MEDICAL DEVICE REW

a clinician’s perspective

INTERNATIONAL MEDICAL DEVICE REGULATORY FORUM (IMDRF) 2017

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Interventional Cardiologist, Schulich Heart Center,
Sunnybrook Health Sciences Center
Scientist, Sunnybrook Research Institute

CADTH
OUTLINE

1. Who am I?
   • Clinician
   • Researcher
   • CADTH

2. What is CADTH?

3. Trans-catheter Aortic Valve Replacement
   • Medical device life-cycle milestones

4. RWE in TAVR – how it happened

5. RWE in TAVR– missed opportunities
Who am I A. clinician

- Interventional cardiologist at Sunnybrook Health Sciences Center, University of Toronto, since 2008

- Clinical practice is restricted to coronary angiography and angioplasty, and TAVR

- TAVR since 2009, with ~150 cases annually (3rd largest in Canada)
Who am I: B. researcher

- Health service researcher at the Institute for Clinical Evaluative Sciences

- Expertise in administrative data for use in health technology assessment
  - Health outcomes
  - Health care costs
  - Integrating these data as inputs in decision analytic economic/policy models
Who I am? Real World Evidence

**CorHealth Ontario TAVI Registry**
- Patient risk factors & clinical characteristics
- Wait-time
- Medications and doses
- Procedural details
- Peri-procedural complications

**Cardiac Services BC TAVI Registry**
- Patient risk factors & clinical characteristics
- Wait-time
- Medications and doses
- Procedural details
- Peri-procedural complications

**CIHI Discharge Abstract Database (DAD)**
- Data: Acute hospitalizations

**National Ambulatory Care Reporting System (NACRS)**
- Data: ED visits & Same day surgeries

**Continuing Care Reporting System**
- Data: Complex continuing care and long term care

**Homecare Database**
- Data: Homecare services

**Ontario Drug Benefit (ODB)**
- Data: Outpatient prescriptions dispensed

**Ontario Health Insurance Plan (OHIP) & BC Medical services Plan (MSP)**
- Data: Physician claims for visits, procedures and diagnostic tests

**CorHealth Ontario TAVI Registry**
- 2012-2017

**Cardiac Services BC TAVI Registry**
- 2012-2017

**Vital Statistics Database**
- Data: Date of Death & Location

**Ontario Drug Benefit (ODB)**
- Age > 65 years

**BC Pharmanet**
- All patients

**Vital Statistics Database**
- Data: Date of Death & Location
Who am I: c. CADTH VP
CADTH is an independent, not-for-profit organization responsible for providing Canada’s health care decision-makers with objective evidence about the optimal use of drugs and medical devices.
Our Programs and Services

**DRUG REIMBURSEMENT RECOMMENDATIONS**
- CADTH Common Drug Review (CDR)
- CADTH pan-Canadian Oncology Drug Review (pCODR)

**HEALTH TECHNOLOGY MANAGEMENT PROGRAM**
- Rapid Response Service
- Health Technology Assessment Service
- Optimal Use Service
- Environmental Scanning
- Horizon Scanning

**OTHER PROGRAMS AND SERVICES**
- Scientific Advice

**KNOWLEDGE MOBILIZATION AND LIAISON OFFICERS**
- Located in jurisdictions across Canada
- Understand the needs and priorities of local decision-makers
- Provide advice and tools to help turn evidence into policy and practice
HEALTH TECHNOLOGY MANAGEMENT PROGRAMS

- Rapid Response Service
- Health Technology Assessment Service
- Optimal Use Service
- Environmental Scanning
- Horizon Scanning
Programs and Services

Knowledge Mobilization and Liaison Officers

- Located in jurisdictions across Canada
- Understand the needs and priorities of local decision-makers
- Provide advice and tools to help turn evidence into policy and practice
CADTH was created to build Canada’s capacity to use evidence as the basis for sound health care decisions. This strategic imperative remains a cornerstone of our work.
Aortic Stenosis Background

- Degenerative valve disease
  - Prevalence of 13.2% in patients >75 years
  - Next cardiovascular epidemic in developed countries
- Severe aortic stenosis (AS) is the most common valvular condition that requires intervention
Latent Period
(Increasing Obstruction, Myocardial Overload)

5-year survival rates

Survival, %

Survival, %

Breast Cancer
Lung Cancer
Colorectal Cancer
Prostate Cancer
Ovarian Cancer
Severe Inoperable AS*

0 5 10 15 20 25 30 35

12
Therapeutic Need

- Surgical Aortic Valve Replacement (SAVR)
  - Traditionally ~ 50% of AS patients ineligible due to excessive peri-operative risk
Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis
First Human Case Description

Alain Cribier, MD; Helene Eltchaninoff, MD; Assaf Bash, PhD; Nicolas Borenstein, MD; Christophe Tron, MD; Fabrice Bauer, MD; Genevieve Derumeaux, MD; Frederic Anselme, MD; François Laborde, MD; Martin B. Leon, MD
TAVR

- Majority are awake
- Fully percutaneous
- Median Length of hospital stay
  - 2 days
Life Cycle of TAVR

- 2002: CE Mark
- 2007: FDA and HC approval
- 2011: Funding in Ontario for inoperable only
- 2012: Funding in Ontario for inoperable only
- 2014: Guidelines for inoperable and high risk
- 2016: Ontario funds high risk
- 2017: Guidelines (intermediate risk)

Market share %

Time

Innovators 2.5 %
Early Adopters 13.5 %
Early Majority 34 %
Late Majority 34 %
Laggards 16 %
RWE in TAVR: how it happened

- Pre-regulatory
- None
- Regulatory approval delayed till publication of landmark PARTNERs trials
RWE in TAVR: how it happened

• Pre-regulatory programs had initiated with foundation funds

• 10 programs in Ontario

• First in 2007
RWE in TAVR: how it happened

• Post-Regulatory
  • Funding 2012
    • No RWE used in decision
    • Mandated that precondition for funding would be mandatory data entry into clinical registry to be held by CorHealth Ontario (CCN)
  • However,
    – No clear a priori objective for data
    – No direction on data elements
    – No funding for data collection
RWE in TAVR: how it happened

- Canadian Cardiovascular Society (CCS) developed quality indicators for TAVR

**STRUCTURAL**
- Heart Team treatment recommendation
- TAVI wait time

**PROCESS**
- Evaluation of procedural risk
- Evaluation of quality of life

**OUTCOMES**
- Mortality for TAVI
- In-hospital stroke post-TAVI
- All cause hospital readmission
RWE in TAVR: as it happened

Province
- Alberta
- British Columbia
- Manitoba
- New Brunswick
- Nova Scotia
- Ontario
- Québec

TAVI Hospitals
- N=2
- N=4
- N=1
- N=1
- N=1
- N=10
- N=6

Approach
- CSBC
- CCN
- INESSS

ICES VPN

CCS National Quality Report: TAVI Dataset
# RWE Data in TAVR: findings

- **Data quality:**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Ontario</th>
<th>Québec</th>
<th>British Columbia</th>
<th>Alberta - Calgary Site</th>
<th>Alberta - Edmonton Site</th>
<th>Manitoba</th>
<th>New Brunswick</th>
<th>Nova Scotia</th>
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<td>Heart Team Recommendation</td>
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<td>Wait time 1</td>
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<td>●</td>
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<tr>
<td>Total wait time</td>
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<td>●</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<td>STS score</td>
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<td>●</td>
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<td>●</td>
<td>●</td>
<td>●</td>
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<td>●</td>
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<tr>
<td>Quality of life pre and 1-year post</td>
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<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>●</td>
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<td>30-day mortality</td>
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<tr>
<td>1-year mortality</td>
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<tr>
<td>In-hospital stroke</td>
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<td>●</td>
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<td>●</td>
<td>●</td>
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<tr>
<td>30-day readmission</td>
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<tr>
<td>1-year readmission</td>
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</table>
RWE in TAVR: findings

- ACCESS
ACCESS

Procedures / million inhabitants in 2015

Cases/million population

Germany: 204
Switzerland: 138
France: 105
Austria: 95
USA: 93
Netherlands: 78
Nordics: 71
Italy: 54
Belgium: 35
UK: 33
Spain: 32
Portugal: 19
Japan: 12

2016
Japan: 25!
Canada

- April 1st 2013- March 31st 2014: 1,136 cases
Valve Centers/Million Population

- US: 1.5
- Germany: 1.25
- Japan: 0.8
- Canada: 0.6
- UK: 0.5
RWE: Access

- Exponentially increasing demand with limited capacity

**Total TAVI wait time**

**Time 1: From Referral to Acceptance**
- Referral
  - “Inappropriate” referral (do not proceed to assessment/work-up):
    - Lack of indications
    - Patient has reasons for not proceeding with assessment
- Assessment
  - Basic requirements:
    - TTE
    - Cardiac catheterization
    - Computed Tomography
    - Consultation with cardiologist and cardiac surgeon
    - Functional assessment
  - +/- Other requirements:
    - TEE
    - Carotid ultrasound
    - Pulmonary function test
    - Additional medical consultations
    - Other diagnostic tests
- Heart Team Decision
  - Meets acceptance criteria:
    - Consensus Heart Team decision
  - Does not meet acceptance criteria:
    - Re-refer to surgery
    - Medical management (“Watchful waiting”)
    - Excessive risk (Palliative referral)
  - Potential for being placed “on hold” during Time 1 or Time 2:
    - Medical reasons
    - Patient preference

**Time 2: From Acceptance to Procedure**
- Placed on Wait List
- Procedure
  - Placed on waitlist:
    1. Procedure planning risk stratification
    2. Urgency assessment
    3. Patient is ready, willing and able
### RWE: Wait-times

<table>
<thead>
<tr>
<th>Canada</th>
<th>Ontario (N=396)</th>
<th>Québec (N=294)</th>
<th>British Columbia (N=270)</th>
<th>Alberta, Manitoba, New Brunswick, Nova Scotia (N=162)</th>
<th>Canada (N=1,122)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Wait Time (median and IQR, days)</td>
<td>105 (58-183)</td>
<td>n/a</td>
<td>91 (57-139)</td>
<td>145 (79-219)</td>
<td>106 (59-172)</td>
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<tr>
<td>Missing data (%)</td>
<td>0.2</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>26.3</td>
</tr>
</tbody>
</table>

- **Canadian Wait-Time Alliance:**
  - Maximum recommended wait-times for surgical aortic valve replacement
    - 14 days for urgent cases
    - 42 days for elective cases
Wait-times

Balance

Increased demand (referrals/cases) =
 Increased capacity (funding)
Wait-time consequences

Wait-time mortality: ~4.5%

Wait-time hospitalization for heart failure: ~15%
Canada

~50% of costs are device related
# Modifiable Drivers of Costs

<table>
<thead>
<tr>
<th>Factor</th>
<th>Rate Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-transfemoral</td>
<td>1.31 (1.18-1.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Length of stay &gt;3 days</td>
<td>1.42 (1.14-1.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Long ICU stay &gt;4 days</td>
<td>1.30 (1.2-1.41)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
RWE in TAVR

• Limited impact on regulatory and reimbursement process

• Substantial insights into implementation and dissemination
RWE in TAVR – missed opportunities

2011 FDA and HC approval

CE Mark 2007

2002

2012
Funding in Ontario for inoperable only

2007 CE Mark

2002

SPECIAL ACCESS
- Earlier initiation
- Define evidentiary needs
- ?Adaptive pathway

Dis-investment?
Reallocation of resources from surgery

Market share %

Time

Innovators 2.5 %
Early Adopters 13.5 %
Early Majority 34 %
Late Majority 34 %
Laggards 16 %

CADTH
Conclusions

• In rapidly changing landscape, early engagement to define the objectives of RWE collection is critical

• RWE is resource intensive
  • Prone to poor quality if front line health care providers are not convinced as to its utility

• Iterative re-evaluations of regulatory and reimbursement decisions, informed by RWE will potentially facilitate earlier, and more efficient dissemination and greater access
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